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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/247,406	02/10/1999	MICHAEL CAPLAN	2002834-0050	7606

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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/247,406	CAPLAN, MICHAEL	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-105* is/are pending in the application.

4a) Of the above claim(s) *98-105* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 89-97 in the reply filed on 1/15/2002 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicants' election of the species peanut allergen proteins, specifically Ara h 1,2 and 3 in the reply of 1/15/2004 and T-cell stimulatory activity (claim 90) for the biological activity in the reply of 4/29/2002 is also noted.

Claims 90, 96 (drawn to the non-elected species) and claims 98-105 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Election was made **without** traverse.

Status of Claims

Claims 89-105 are pending in the application.

Claims 90, 96 (drawn to the non-elected species) and claims 98-105 are withdrawn from further consideration pursuant to 37

CFR 1.142(b) as being drawn to a nonelected invention and species.

Claims 89-97 are under examination.

Specification

The abstract of the disclosure is objected to because it is too long. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of ***50 to 150 words***. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 89-97 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth

the claimed invention. Lockwood v.American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The specification, at the time of filing, does not describe the full scope of the huge genus. The claims recite for a collection of mutant allergen genes that are different in sequences from a gene encoding a naturally occurring allergen protein by one or more nucleotide deletion, addition or substitution. The specification provides only definitions for each of the components of the method. The claimed allergen, for example, covers all or any kind of the same or different type of allergens such as foods, pollens, dusts and etc. Even if the allergen is limited to food alone, there are numerous types of allergens against food. The specification does not provide the method by which the collection of mutant allergen from any single allergen is described. It is not apparent from the general description and statement from the specification of any allergen that has been employed in the method. Not a single example has been provided to describe in detail the claimed method. While example, may not be required for a predictable art as mechanical art, however, in a highly unpredictable art as biotechnology said example is almost a must. In biotechnological invention one cannot necessarily claim a genus after only describing a single species (in the instant case, not a single species is described) because there may be unpredictability in

the results obtained from species other than those specifically described. The statements provided in the specification are nothing more than generalizations or summations of what is presumed to be knowledge present in the prior art. However, the general knowledge in the art, at the time of applicants' invention, is such that no generalization has been made in such a complex matter as allergen. This is because there is not one kind of reagent that can treat different kinds of allergens even for different food allergen. Allergens are so vast, diverse and complex that study to date still remains obscure since an individual's response for an allergen varies widely and unpredictably. Posch et al (J. Allergy Clin. Immunol.) e.g., at page 391, col. 2 recites that "...the role of the novel IgE-binding proteins with respect to latex allergy cannot be assessed at the moment, because pure allergens are required for detailed studies in vitro and in vivo..." Furthermore, at page 394, col. 1, Posch states that "the IgE reaction profiles obtained for health care workers with latex allergy may be different from those of patients with spina bifida and therefore cannot be generalized..." (Emphasis added). Likewise, Alenius(Clinical and Experimental Allergy) at e.g., page 664 states that "..the information from the primary structures of significant allergens such as proheivein in latex allergy, can be used for the identification and localization of allergenic

epitopes. This knowledge provides tools for the production of substantial amounts of relevant antigens for diagnostic purposes, 'which at present in latex allergy are not based on standardized allergens..." Trials utilizing immunogenic peptides representing T cell epitopes have been disappointing. The claims drawn to said method does not have a corresponding written description so specific as to lead one to the claimed method.

To satisfy a written description requirement for a claimed genus a sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. A representative number of species means that the species, which are adequately described, are representative of the entire genus. A listing (definition) of every possible components in a single component in the claim does not constitute a written description of every species in a genus. It would not reasonably lead those skilled in the art to

any particular species. In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

Applicants, at the time of filing, are deemed to have not invented species sufficient to constitute the genus, the evidence indicates ordinary artisans could not predict the operability in the invention based only on general statements.

Claims 89-97 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(1) the breadth of the claims,
(2) the nature of the invention,
(3) the state of the prior art,
(4) the level of one of ordinary skill;
(5) the level of predictability in the art,
(6) the amount of direction provided by the inventor,
(7) the existence of working examples, and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, (U.S.P.Q. 2d 1400 (CAFC 1988).

1). The specification fails to give adequate direction and guidance in how to readily go about determining which allergen genes from numerous allergens the ones that undergo mutations. Whether the type of mutations (substitution, deletion or addition) is singly or in combinations. The kind of nucleotide or location in the parent allergen genes that is mutated. The number of allergens present in a collection, the type of host cell or vector use in the expression and/or assay to detect reduction to anti-allergen IgE.

2). The specification failed to provide a single working example for the numerous and different type of allergen genes, vectors, host cells, and other undefined variables present in the claimed method.

3). The breadth of the claims encompasses a large diversity of allergens, let alone its mutants. It is well known in the art that the diversity of the inserts (allergen mutants) in a vector or host is not easily estimated. It may be for example, that only a small subset of possible peptide sequences encoded by the allergen genes are presented efficiently by a particular expression system. And, it is not always easy to follow the expression of encoded peptides in particular cells; for example, to know whether or not a specific cell is

expressing a member of the insert, especially for biological methods.

4). The state of the prior art is such that techniques or methods are specifically applied or adapted for a known or defined structure of a specific fragment of a specific allergen genes and/or its mutant.

5). The art is inherently unpredictable because it is not possible to predict that even with a predetermined sequenced of allergen genes, the nucleotide that can be mutated by the different means of modifications the ones that would exhibit the desired reduction of anti-IgE binding. Furthermore, it is generally known that there are still no rules that have emerged that allow structure to be related to sequence in any simple fashion (even as applied to the actual compounds).

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art to the numerous undefined variables of the claimed method. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 89-90 and 94-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 29-31 of copending Application No. 10/100,303. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant broad claimed method encompasses the specific method of the '303 application reciting the at least one specific mutant.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 89 and 91-95 are rejected under 35 U.S.C. 102(a) as being anticipated by Hakkaart et al (Allergy).

Hakkart disclose at e.g., page 166, col. 1, "Materials and Methods" up to page 170, col. 1 and page 171, col. 1 a method comprising of mutanizing the house-dust-mite allergen, Der p 2 by replacing the Cys residues with Ala by the method of cDNa that generates a collection of fragments of Der p2 mutants and then identifying the fragments that are monospecific to the mab produced from immunization of mice wherein the characteristic of the mutants still possessed the ability to induce histamine release from basophilic leukocytes. The specific process steps

of Hakkaart utilizing the specific allergen in the process steps to identify those mutants that immunoreact with antibodies fully meets the instant broad process steps for any kind of protein mutations.

Claims 89 and 91-95 are rejected under 35 U.S.C. 102(b) as being anticipated Smith (J. Allergy and Clin. Immuno.).

Smith discloses a method comprising of mutanizing the house-dust-mite allergen, Der p 2 by deleting e.g., the Cys 73-38 bond residues with Ala by the method of cDNa that generates a collection of fragments of Der p2 mutants and then identifying the fragments that are monospecific to the mab produced from immunization of mice wherein the characteristic of the mutants still possessed the ability to induce histamine release from basophilic leukocytes. The specific process steps of Smith utilizing the specific allergen in the process steps to identify those mutants that immunoreact with antibodies fully meets the instant broad process steps for any kind of protein mutations. See the entire abstract.

Claims 89 and 91-95 are rejected under 35 U.S.C. 102(b) as being anticipated by Jespers et al (The. Jrnl. Mol. Biol.).

The broadly recited method comprising providing a collection of mutant polypeptide wherein the amino acid sequence

of each mutant polypeptide differs in at least one position from a polypeptide of interest, and identifying the mutant polypeptide within the collection that have an alteration in antibody reactivity compared to the polypeptide of interest and retain at least one desired characteristic, wherein alteration in the antibody reactivity is determined by exposing he mutant polypeptide to individual antibodies or antibody fragments that are monospecific for the polypeptide of interest is fully met by the process step of Jespers at e.g., page 704. Jespers disclose a method wherein a library of randomized antigen variants containing most single, double and triple amino acid mutants generated by single nucleotide substitutions is produced by error-prone PCR amplification of the DNA sequence encoding the protein antigen. The phage -displayed library is then selected fro epitope mutants by passing through an affinity matrix derivatized with a specific antibody and positively selected for retention of function.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the

> differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 89-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Williams et al (Jrnl. Of immunological methods) in view of Stanley et al (Archives of Biochemistry and Biophysics).

Williams discloses at page 4, 2.6 up to 15 a method of identifying a mutant from two different epitopes from the beta lactoglobulin(BLG) allergen that bind to IgG antibodies comprising using random peptide (mutation by substitution or addition) fused to the filamentous phage pVIII and then screening the phage library by contacting with IgG. Williams does not disclose screening against IgE or the allergen, as the elected peanut, Ara h. However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to screen the epitope allergen BLG against IgE since it is well known in the art that allergens are known or characterized by both humoral (IgG and IgE) and has cellular T-cell binding sites. Furthermore, it would have been obvious to use peanut as the allergen in the method of Williams as taught by Stanley (page 244). Peanuts are a major cause of serious allergic reactions in both children and adults. The

hypersensitivity to peanuts often starts in childhood and continues throughout life. While milk (BLG) generally resolve spontaneously with age. This would provide the motivation to one having ordinary skill in the art i.e., to find the allergen (mutant) in peanuts and find treatment for peanut allergy.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Bannon discloses methods and reagents for decreasing clinical reaction to allergy.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
June 13, 2005